Assessing peripheral arteries in South African black women with type 2 diabetes mellitus

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Objectives. To determine the value of ankle and toe blood pressure indices and pedal pulse palpation in the assessment of peripheral arterial disease in subjects with type 2 diabetes mellitus (DM).

Design. Cross-sectional study.

Subjects. A convenience sample of 85 female subjects with type 2 DM underwent a series of peripheral vascular assessments at the diabetes clinic of a community hospital.

Outcome measures. Palpation of the pedal pulses, Doppler-derived ankle brachial systolic blood pressure indices, photo plethysmographic-derived toe brachial systolic blood pressure indices and antero-posterior radiographs of both feet.

Results. Mean values were 1.15 (standard deviation (SD): 0.17) and 0.76 (SD: 0.17) for ankle brachial index (ABI) and toe brachial index (TBI) respectively. The differences between the two indices increased from 0.36 (95% confidence interval (CI): 0.32 - 0.41) to 0.58 (95% CI: 0.46 - 0.70) depending on whether ABI was less or greater than 1.3. The correlation coefficient for left versus right foot was 0.62 and 0.71 for ABI and TBI respectively. The relationship between ABI and TBI is non-linear with a cut point close to 1.3. Both ABI and TBI were significantly lower in subjects who had both pedal pulses absent on palpation.

Conclusions. The relationship between ABI and TBI is linear below an ABI of 1.3. but with a wide 95% prediction interval. If both pedal pulses are absent the ABI is significantly diminished compared with when both pulses are present, even though not necessarily below 0.9.

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Peripheral vascular disease is 2 - 3 times more likely to develop in people with diabetes mellitus (DM) than in the general population.[1] It can occur in 8% of people at the time of diagnosis of DM and may reach 45% by 20 years' duration.[2]

There are no published data on the prevalence of peripheral artery disease (PAD) or medial arterial calcification in an unselected group of black South African patients with DM. Traditionally it is thought that South African blacks have a lower incidence of vascular disease than their white counterparts. In the studies[3,4] examining PAD as seen in a vascular unit in Durban the pattern of atherosclerotic disease varied between the different ethnic groups reviewed, with black patients suffering more from peripheral aneurysms than aortic aneurysm and generally having more limb-threatening peripheral vascular disease than exercise-limiting claudication. The black population generally had a higher concentration of high-density lipoproteins than the white or Indian populations. The black patients presented much later in the process than the other population groups. PAD is therefore well established in blacks but the incidence is still lower compared with that of other ethnic groups. The reason for these differences still needs careful investigation.

The screening evaluation of the foot of a person with DM should include palpation of pedal pulses and if pulses are absent or decreased a more specific vascular evaluation is indicated (particularly if the tibialis posterior pulse is absent).[2] In general, this means a Doppler evaluation of ankle and brachial systolic pressures defined as an ankle brachial index (ABI) with ratio less than 0.9 indicating peripheral vascular disease. Because medial arterial calcification can cause falsely elevated pressures some advocate the use of toe systolic blood pressure indices in subjects with DM.[2] At least one study has shown that in the absence of overt calcification (ABI ≥ 1.3) the toe systolic blood pressure indices convey no advantage over ABI in determining perfusion pressure of the lower limbs.[5]

No data are available on this topic in African black diabetic patients, where the prevalence would probably be lower and the value of the ABI in these patients is still regarded as questionable. Therefore, the aim of our study was to determine the concordance between ankle Doppler indices and toe systolic blood pressure indices as well as to determine the value of pedal pulse palpation in the assessment of PAD.

Methods

The setting for this cross-sectional study was Mamelodi Hospital, a community hospital serving mainly as a primary health care facility for the urban black community of

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approximately 500 000 people. Included in the study were patients previously diagnosed with DM. Owing to the relatively small number of men and type 1 subjects seen at the clinic, the study was restricted to women with type 2 DM (diagnosed after the age of 30 years and insulin not used within the first year of diagnosis). The subjects were invited to participate from the waiting room of the diabetes clinic (held twice a week).

Measurements

All subjects fasted for at least 10 hours before a venepuncture was performed and the samples were then transported on ice to the laboratory. Serum glucose and HbA_{1c} were determined using a Beckman LX20.

A sitting non-weight-bearing bilateral antero-posterior X-ray of both feet was done for each patient. The films were examined for arterial calcification by a radiologist who was blinded to the clinical data. Linear calcification in any artery was categorised as medial arterial calcification, and any patchy calcification was classified as intimal arterial calcification. Radiographs with both intimal and medial calcification were categorised as medial arterial calcification (in either foot), while those that were indeterminate or only found to have intimal calcification were categorised as not having medial arterial calcification.[6]

A trained observer, asking all relevant questions, completed a general questionnaire regarding smoking status, alcohol consumption, education status, hypertension status, all treatment and menopausal state. The Rose questionnaire[7] was used to determine angina and grade of angina, grade of dyspnoea and grade of intermittent claudication if present.

Weight was determined to the nearest 0.1 kg standing barefoot in light clothing on a calibrated electronic scale (Tanita, Tokyo). Height was determined to the nearest 0.1 cm using a measuring stick attached to the wall. Body mass index (BMI) was calculated as weight/height in m^2. Blood pressure was measured in the sitting position after at least 5 minutes' rest, with the right arm resting on a table, using a mercury sphygmomanometer and a large cuff if mid-arm circumference exceeded 33 cm. Hypertension was noted if patients were on antihypertensive medication.

The feet were examined by two trained medical students and the dorsalis pedis and tibialis posterior arteries were palpated (using a standardised protocol). The foot examiners were blinded as to the Doppler and plethysmography measurements. A continuous wave Doppler system (Multi Dopplex, HNE Diagnostics, Cardiff) was used by a single examiner (JTvW) to measure systolic pressures. The procedure as set out by a consensus document was strictly adhered to.[2] The means of duplicate measurements of dorsalis pedis and tibialis posterior were used for calculation of the ABI. The higher of the two indices was used as the ABI for a given foot.[8] An ABI less than 0.9 was used to define peripheral vascular disease.[8]

Photo plethysmography (Hokanson, Washington) was used to measure toe systolic blood pressure. Before taking two measurements, on the left and right hallux, one measurement was taken as a reference. To obtain the toe brachial index (TBI) a Doppler systolic blood pressure measurement of the brachial artery was performed at the same time as the plethysmography measurements. A TBI less than 0.6 was used to define peripheral vascular disease.[2] A single observer took all the vascular measurements.

Before the study the intra-observer variance of Doppler-derived indices was determined on 28 feet and found to be 8.13% in the right foot and 8.90% in the left foot. Regarding photo plethysmographic toe indices, the intra-observer variance was tested on 19 feet and was 13.07%.

Data analysis

Data analysis was done using Stata 8. Descriptive statistics included means and standard deviations (SDs) for parametric data and medians with 25th and 75th quartiles for non-parametric data. Pearson's correlation coefficients were calculated to define the relationship between the vascular measurements. Concordance was evaluated using the Kappa statistic (κ). It has a maximum of 1.00 when agreement is perfect, a value of zero indicates agreement no better than chance, and negative values show worse than chance agreement. A kappa value less than 0.20 indicates poor agreement, 0.21 - 0.40 fair agreement, 0.41 - 0.60 moderate agreement, 0.61 - 0.80 good agreement, and greater than 0.80 very good agreement.[9]

Results from both legs were combined in the analyses for a mean ABI and mean TBI. Differences between mean ABI and mean TBI were compared using an unpaired *t*-test. Linear regression as well as fractional polynomial regression were used to determine the best transformation of ABI to predict TBI.

To compare the ABI and TBI across groups, analysis of variance (ANOVA) was used with a Scheffe correction on *post hoc* testing. If data did not comply with assumptions for ANOVA, Kruskal-Wallis tests were performed with *post hoc* testing correcting for multiple testing. A non-parametric trend test was used to determine a trend in indices across number of absent pulses in each foot. A two-sided p-value < 0.05 was regarded as statistically significant.

Results

Of the 134 women invited, 112 agreed to participate (85%); 93 came to the first evaluation (69%) and 88 to the second (66%)

Table I. Characteristics of the study group (*N* = 85)

	Mean (SD)
Age (years)	58.52 (8.21)
Systolic blood pressure (mmHg)	150.73 (26.20)
Diastolic blood pressure (mmHg)	89.11 (11.52)
Body mass index (kg/m^2	31.95 (5.23)
Duration of diabetes* (years)	6.00 (3.00, 12.00)
Serum glucose* (mmol/l)	9.80 (7.10, 14.30)
HbA_{1c} (%)	9.78 (2.26)
Post-menopausal (*N* (%))	66 (77.7)
History of stroke† (*N* (%))	7 (8.2)
Angina† (*N* (%))	10 (11.8)
Intermittent claudication† (*N* (%))	5 (5.9)
Vascular measurements (mean (SD))	
ABI right (*N* = 85)	1.16 (0.21)
ABI left (*N* = 83)	1.15 (0.15)
Mean ABI (*N* = 85)	1.15 (0.17)
TBI right (*N* = 83)	0.76 (0.20)
TBI left (*N* = 82)	0.78 (0.16)
Mean TBI (*N* = 83)	0.76 (0.17)

*Median (25th, 75th percentile).
†According to the Rose questionnaire.
ABI = ankle brachial index; TBI = toe brachial index.

which was the vascular assessment. Blood samples and vascular measurements (63.4%) were complete in 85 patients, urine analysis in 78 and X-rays of the feet in 92. The characteristics of the women who completed the vascular examination are given in Table I. The mean age was 58.5 (8.2) years and the mean BMI 32.0 (5.2) kg/m^2. The 8 women who did not return were not statistically significantly different with regard to age ($p = 0.40$), BMI ($p = 0.96$) or waist circumference ($p = 0.40$). They had diabetes of shorter duration (median 3.0 years, $p = 0.06$).

The vascular measurements are described in Table I. The values were distributed normally, with the mean toe systolic indices being approximately 66% of the mean ABIs. The Pearson's correlation coefficients between the different indices were as follows: for ABI right and ABI left 0.62 ($p < 0.001$) and for TBI right and TBI left 0.71 ($p < 0.001$). The relationship between the left and right index is shown in Fig. 1. The TBI of the right foot explains 51% of the variation in values in the left foot whereas the ABI of the right foot only explains 38% of the variation in the left foot values. However, as can be seen in Fig. 1, the 95% prediction interval of Y given a particular value of X is probably too wide from a clinical point of view for both ABI and TBI. The relationship between the mean of each subject's ABI and the mean of TBI is not linear and correlations were not calculated. Examination of the residuals of a regression line fitting ABI against TBI shows that a linear function is inappropriate. Fractional polynomial regression revealed that the best model (according to the r^2) was obtained

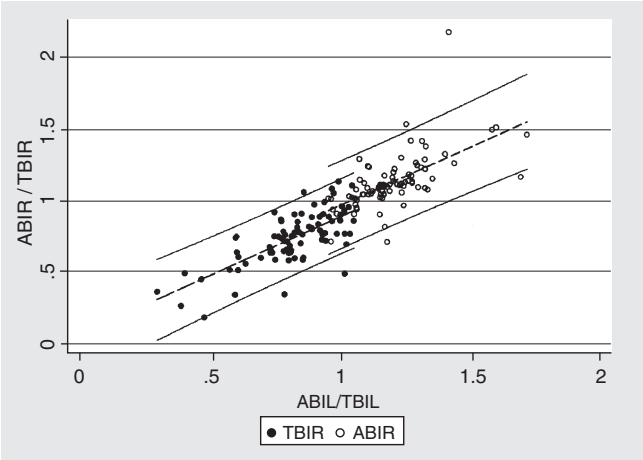

Fig. 1. Scatter plot of ankle brachial index (ABI) left versus ABI right and toe brachial index (TBI) left versus TBI right with predicted values (straight line) and the 95% prediction interval (r^2 for ABI 0.38 and for TBI 0.51).

when a cubic transformation of ABI was used (with one extreme outlier excluded, the r^2 was 0.30 and the coefficient for the transformed ABI was –0.47 (95% CI: –0.63 - –0.31) for predicting TBI) (Fig. 2). Fractional polynomial regression yielded best fit with untransformed ABI if ABI was < 1.26 whereafter a cubic transformation showed best fit of the data. Even though the relationship between ABI and TBI is approximately linear when ABI is < 1.3, the 95% prediction interval is wide (Fig. 3)

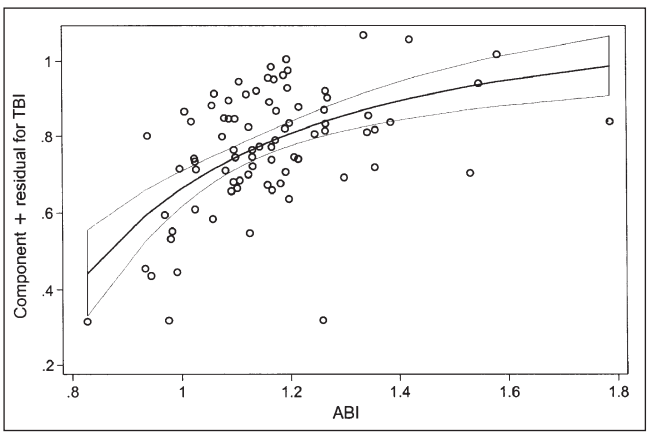

Fig. 2. Scatter plot of mean ankle brachial index (ABI) versus mean toe brachial index (TBI) with predicted values (straight line) and the 95% CI based on a cubic transformation of ABI.

The mean difference between ABI and TBI was 0.36 (95% CI: 0.32 - 0.41) if those with ABI ≥ 1.3 were excluded (*N* = 72). If only subjects with ABI ≥ 1.3 were used (*N* = 11) then the mean difference was 0.58 (95% CI: 0.46 - 0.70).

For the evaluation of PAD we kept the left and right foot measurements separate. We found a prevalence of PAD (based

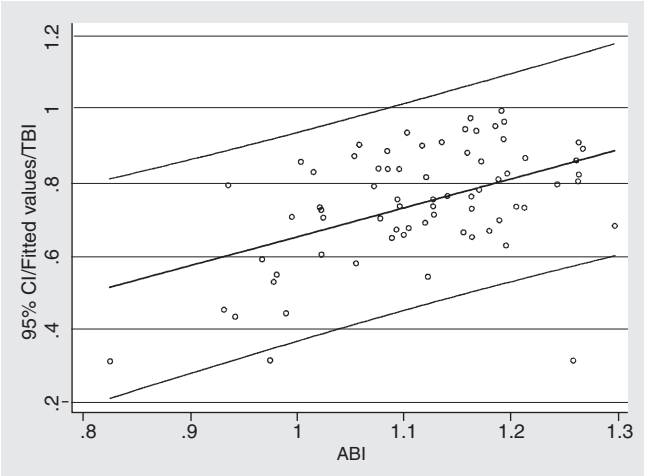

Fig. 3. Scatter plot of ankle brachial index (ABI) versus toe brachial index (TBI) if ABI is < 1.3 with the predicted values (straight line) and the 95% prediction interval.

on ABI < 0.9) of 4.7% (4/86) in the right foot and none in the left foot. If based on TBI (< 0.6), then the prevalence of PAD was 14.5% (12/83) in the right and 15.9% (13/82) in the left foot. The small numbers preclude judgement on concordance between PAD diagnosis using ABI and TBI. More subjects were diagnosed as having PAD with TBI than with ABI ($p = 0.04$ for right foot and $p < 0.01$ for left foot).

Eight (9.9%) of 81 subjects had radiological evidence of medial arterial calcification. An ABI of > 1.3 is commonly regarded as indicative of medial arterial calcification. We found very poor concordance between radiological medial arterial calcification and ABI > 1.3. For subjects with ABI > 1.3 the kappa value was 0.11 ($p < 0.001$). For subjects with medial arterial calcification versus without, the mean ABI was 1.15 (0.15) v. 1.18 (0.13) ($p = 0.83$) and mean TBI 0.76 (0.16) v. 0.73 (0.28) ($p = 0.81$).

Five subjects (5.9%) had intermittent claudication according to the Rose questionnaire. None of these had both pedal pulses absent in either left or right foot. Only 1 of these subjects had a (left or right) ABI < 0.9. Two patients had either a left or right TBI < 0.6. One had an ABI > 1.3. If an abnormal index is defined as ABI < 0.9 or > 1.3 or TBI < 0.6, then 3/5 (60.0%) had an abnormal index compared with 27/80 (33.8%) of those without intermittent claudication ($p = 0.34$).

In Table II Doppler indices are given as continuous measurements dependent on the number of pulses absent in each foot. Both indices decreased as the number of pulses decreased in each foot. It is clear from the table that the greatest difference occurs between those feet with two absent pulses versus one or none absent. On *post hoc* testing 0 v. 2 pulses absent were significantly different for ABI right, ABI left and TBI left (adjusted p-values < 0.05).

Discussion

Our relatively small study demonstrates some of the problems regarding vascular evaluation in DM. The prevalence of PAD as defined by an ABI < 0.9 is low as could be expected in an unselected group of black South African women with DM. There was a low prevalence of medial arterial calcification (9.9%) and this did not correlate with an ABI > 1.3.

The indices based on photo plethysmographic-derived toe blood pressures were on average 34% lower than the Doppler-derived ankle indices. As expected, there was a positive correlation between the left and right indices, with the toe indices showing the strongest correlation. However, the wide prediction intervals probably preclude their interchangeable use.

In the clinical setting the ABI is often used before more invasive testing such as angiography. It has predictive value for delayed wound healing[10] and amputation.[11] An ABI < 0.9 is 95% sensitive and almost 100% specific in detecting angiogram-positive disease.[12] Critical ischaemia is defined by an ABI < 0.5.[13] The variability of ABI can be attributed mainly to biological variability and to a lesser extent to observer

Table II. Indices dependent on number of absent pulses (mean (SD))

Number of absent pulses	*N*	Ankle brachial index right	*N*	Ankle brachial index left	*N*	Toe brachial index right	*N*	Toe brachial index left
0	31	1.20 (0.23)	22	1.16 (0.09)	30	0.76 (0.19)	22	0.80 (0.14)
1	47	1.17 (0.18)	52	1.17 (0.16)	47	0.79 (0.18)	52	0.78 (0.12)
2	7	0.93 (0.14)	9	1.04 (0.11)	6	0.53 (0.23)	8	0.56 (0.27)
p-value		0.001		0.03		0.05		0.04
Trend *p*-value		0.01		0.02		0.39		0.03

variation.[14] The European Society of Vascular Surgeons prefers the absolute blood pressures of the ankle and toe instead of the ABI.[13]

An expert consensus conference recommended that a screening ABI be performed on all people with type 1 DM ≥ 35 years old or with ≥ 20 years' duration of DM, and for all people with type 2 DM and aged > 40 years.[2]

A toe blood pressure measurement overcomes the false elevation of ankle blood pressures due to calcification and has a similar repeatability to the ABI. In diabetic foot lesions a toe systolic blood pressure < 20 mmHg was associated with a healing rate of only 29% for ulcers compared with a healing rate of 92% for subjects with a toe systolic blood pressure of ≥ 30 mmHg.[2]

In this study we find as expected better agreement between ABI and TBI if ABI is < 1.3. However the prediction interval for any given value is wide. Unfortunately our sample was too small to determine whether despite the last-mentioned limitation either method would predict PAD to the same extent. Interestingly, we found a larger proportion of patients with low TBI compared with low ABI.

PAD is more common in people with DM than in those without; however, the detection of lower extremity arterial disease in clinical practice remains a challenge. In our study the Rose questionnaire defined intermittent claudication in only 5 subjects (5.9%). The number of subjects with PAD is too few to draw any conclusions regarding the value of the Rose questionnaire for intermittent claudication. In a study by Criqui *et al*.[15] (mainly using middle-aged white participants) the sensitivity of the Rose questionnaire for detecting lower extremity arterial disease was 9%, and only 20% of subjects with lower extremity arterial disease had exercise-induced calf pain not present at rest.

Palpation of the foot pulses is greatly affected by room temperature, biological variation and provider skill. The kappa values for absence of pulses of 0.3 - 0.6 can be improved to 0.6 - 0.7 with training and practice.[16,17] In a non-diabetic population the sensitivity/specificity of decreased or absent posterior tibial pulse was 71/91% for an ABI ≤ 0.9.[15]

The study by Brooks *et al*.[5] in an Australian population found the mean differences between ABI and TBI in diabetic subjects to be similar to ours, namely 0.37 (SD 0.15). They also found that nearly all diabetic patients with an ABI < 1.3 have an ABI-TBI gradient falling within the normal range established from a non-diabetic cohort and that in contrast, the majority of diabetic subjects with an ABI ≥ 1.3 have ABI-TBI differences outside this range. When patients are categorised according to ABI and TBI, there is also good agreement between the tests when ABI is low or normal (84% and 78% agreement, respectively), but not when ABI is elevated. Our study differs from theirs, in that as expected our group of patients had less PAD (ABI < 0.9) than did their group (2.4% v. 14.4%, $p = 0.004$). Of interest, however, was that 4/11 (36.0%) of those with high ABI also had high TBI ($p = 0.01$), whereas there was no high TBI associated with high ABI in the Brooks study.[5] This raises the interesting possibility that calcification of the smaller toe vessels may be more prevalent in our study population.

Our study was not designed to specifically evaluate the Rose questionnaire and its value in our setting is still undetermined. It is clear, however, that subjects who have both pedal pulses absent have diminished ABI indices (even if this is not yet < 0.9).

In conclusion, our study supports the need for clinical palpation of the pedal pulses as well as the need for caution in the interpretation of ABI if ABI > 1.3 in the evaluation of vascular status in subjects without specific vascular symptoms.

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References

1. Kannel WB, McGee DL. Diabetes and cardiovascular disease: the Framingham Study. *JAMA* 1979; **241:** 2035-2038.
2. Orchard TJ, Strandness DEJ. Assessment of peripheral vascular disease in diabetes. Report and recommendations of an international workshop sponsored by the American Heart Association and the American Diabetes Association 18 - 20 September 1992, New Orleans, Louisiana. *Diabetes Care* 1993; **16:** 1199-1209.
3. Robbs JV. Atherosclerotic peripheral arterial disease in blacks – an established problem. S *Afr Med J* 1985; **67:** 797-801.
4. Maharaj RR. An inter-racial study into the pattern and prevalence of artherosclerotic peripheral vascular disease in the university based Vascular Surgical Service in Durban. MD thesis, University of Natal, 1999.
5. Brooks B, Dean R, Patel S, Wu B, Molyneaux L, Yue DK. TBI or not TBI: that is the question. Is it better to measure toe pressure than ankle pressure in diabetic patients. *Diabet Med* 2001; **18:** 528-532.
6. Lindbom A. Arteriosclerosis and arterial thrombosis in the lower limb: a roentgenological study. *Acta Radiol (Diagn)* 1950; Suppl 80: 38-48.
7. Rose GA, Blackburn H, Gillum RF, Prineas RJ. *Cardiovascular Survey Methods*. Geneva: World Health Organisation, 1982.
8. Donnely R, Hinwood D, London NJM. Non-invasive methods of arterial and venous assessment. *BMJ* 2000; **320:** 698-701.
9. Altman DG. Some common problems in medical research. In: *Practical Statistics for Medical Research*. London: Chapman and Hall, 1994; 403-409.
10. Pecoraro RE, Ahroni JH, Boyko EJ, Stensel VL. Chronology and determinants of tissue repair in diabetic lower-extremity ulcers. *Diabetes Care* 1991; **40:** 1305-1313.
11. Holstein P. The distal blood pressure predicts healing of amputations on the feet. *Acta Orthop Scand* 1984; **55:** 227-233.
12. Fowkes F. The measurement of atherosclerotic peripheral arterial disease and epidemiologic surveys. *Int J Epidemiol* 1988; **17:** 248-254.
13. European Society of Vascular Surgery. Chronic critical leg ischaemia. *Eur J Vasc Surg* 1992; **6:** 1-3.
14. Mayfield JA, Reiber GE, Sanders LJ, Janisse D, Pogach LM. Preventive feet care in people with diabetes. *Diabetes Care* 1998; **21:** 2161-2177.
15. Criqui MH, Fronek A, Klauber MR, Barrett-Connor E, Gabriel S. The sensitivity, specificity, and predictive value of traditional clinical evaluation of peripheral arterial disease: results from noninvasive testing in a defined population. *Circulation* 1985; **71:** 516-522.
16. Lawson IR, Ingman SR, Masih Y, Freeman B. Reliability of palpation of pedal pulses as ascertained by the kappa statistic. *J Am Geriatr Soc* 1980; **28:** 300-303.
17. Brearley S, Shearman CP, Simms MH. Peripheral pulse palpation: an unreliable physical sign. *Ann R Coll Surg Engl* 1992; **74:** 169-171.

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